

**Table 1. Management of Bronchiolitis in Infants and Children: Inclusion and Exclusion Criteria**

Category	Criteria
Study population	Humans Infants and children
Study settings and geography	Inpatient, outpatient, home; all geographical locations subject to publication language and study design criteria
Time period	Systematic reviews, from 1966 through 2001 Individual studies, published from 1980 through 2001
Publication languages	English only
Admissible evidence (study design and other criteria)	Original research studies that provide sufficient detail regarding methods and results to enable use and adjustment of the data and results  <u>For studies on diagnosis</u> Randomized controlled trials (RCTs): double-blinded, single-blinded, and cross-over designs Non-RCTs: prospective cohort studies  <u>For studies on treatment and prophylaxis:</u> RCTs: double-blinded, single-blinded, and cross-over designs  <u>For the cost-effectiveness component</u> Studies that use an analytical method (e.g., cost, cost-effectiveness, cost-utility, or cost-benefit analysis)  Patient populations must include infants and children Relevant outcomes must be able to be abstracted from data presented in the papers  Sample sizes must be appropriate for the study question addressed in the paper; single case reports or small case series (fewer than 10 subjects) will be excluded

**Table 2. Management of Bronchiolitis in Infants and Children: Search Terms**

<b>Topic</b>	<b>Search terms</b>
Exploded terms for diagnosis	Bronchiolitis, diagnosis, differential diagnosis, thoracic radiography, laboratory techniques and procedures
Exploded terms for treatment	Steroidal anti-inflammatory agents, steroids, bronchodilator agents, antiviral agents, antimicrobial cationic peptides, antibiotics, antimicrobials, anti-infective agents
Exploded terms for prophylaxis	Primary prevention, immunoglobulins, bronchiolitis [prevention & control], isolation strategies, patient isolation
Exploded terms for cost-effectiveness	Costs and cost analysis
Study design for diagnosis	Prospective studies, longitudinal studies, cohort studies
Study design for treatment and prophylaxis	Randomized controlled trial, single-blind method, double-blind method, random allocation, meta-analysis
Outcomes for diagnosis	Fatal outcome, outcome and process assessment (health care), outcome assessment (health care), treatment outcome
Outcomes for treatment and prophylaxis	Morbidity, mortality, adverse effects or harms
Limiting terms for all	Human, year = 1980 through 2001, newborn infant (birth to 1 month) or infant (1 to 23 months) or preschool child (2 to 5 years)

**Table 3. Electronic Databases for Literature Searches**

Database	Description
MEDLINE®	MEDLINE®, maintained by the National Library of Medicine (NLM), is the premier bibliographic database. Its 9.2 million records (with 31,000 new records added weekly) contain articles from more than 3,800 international biomedical journals (some chapters and articles from selected monographs are found in earlier years) covering the field of medicine, nursing dentistry, veterinary medicine, and the preclinical sciences. MEDLINE® contains citations for articles published in all languages from 1966 through the present; these citations are searchable, using NLM's controlled vocabulary, MeSH (Medical Subject Headings). For articles published in a foreign language, English abstracts are provided for 76 percent.
Cochrane Collaboration Resources	Among the Cochrane Collaboration resources are the Cochrane Controlled Trials Register, an electronic database providing reference information on RCTs and other controlled clinical trials in health care. Studies appearing in this database are part of systematic reviews conducted by various Cochrane Collaborative Review groups; all their studies have been reviewed for quality and additional information has been obtained from the original authors or through hard searches of the literature. The Cochrane Library houses the York Database of Abstracts of Reviews of Effectiveness (DARE), which provides access to structured abstracts of systematic reviews, American College of Physicians Journal Club abstracts, abstracts of reports prepared by the members of the International Network of Agencies for Health Technology Assessment, and other systematic reviews.
Health Economic Evaluations Database (HEED)	HEED provides structured summaries (reviews) of more than 20,000 articles appearing in the literature relevant to the economic assessment of health technologies. Each month electronic databases, leading journals and academic/government center publication lists are searched for relevant articles. An expert panel of academic reviewers complete the reviews of articles meeting specific inclusion criteria for cost analyses

**Table 4. Studies Examining the Accuracy of Virologic Tests**

Author	"Gold Standard" <sup>a</sup>	Tests compared <sup>b</sup>	Results <sup>c</sup>
Ahluwalia et al., 1987 <sup>26</sup>	Viral culture of NPA and NPS	EIA, IFA on both NPA and NPS specimens	EIA-NPA: Sn = 69, Sp = 100 EIA-NPS: Sn = 61, Sp = 100 IFA-NPA: Sn = 61, Sp = 89 IFA-NS: Sn = 52, Sp = 78
Chattopadhyaya et al., 1992 <sup>27</sup>	Viral culture	IFA, EIA, EIA by blocking test	IFA: Sn = 89, Sp = 92 EIA: Sn = 94, Sp = 74 EIA by blocking test : Sn = 94, Sp = 77
Eugene-Ruellan et al., 1998 <sup>28</sup>	Viral culture and/or IFA	PCR	97% "concordance"
Ong et al., 2001 <sup>29</sup>	IFA	PCR	IFA detected 27 cases PCR detected 28 cases
Waner et al., 1990 <sup>30</sup>	Viral culture and/or IFA	EIA	Sn = 86, Sp = 91

<sup>a</sup>NPA, nasopharyngeal aspirate; NPS, nasopharyngeal suction; IFA, direct immunofluorescence assay.

<sup>b</sup>EIA, enzyme immunoassays; PCR, polymerase chain reaction.

<sup>c</sup>Sn, sensitivity; Sp, specificity.

**Table 5. Studies Measuring Predictors Of Disease Severity**

<b>Author</b>	<b>Outcome predicted<sup>a</sup></b>	<b>Indicators examined<sup>b</sup></b>	<b>Predictors</b>
Cherian et al., 1997 <sup>34</sup>	Diagnosis of ALRI (based on abnormal findings on auscultation or CRX) using respiratory rate and subcostal retractions in undernourished infants and children with respiratory infections in India	<ul style="list-style-type: none"> <li>• RR <math>\geq 60</math>/min in infants &lt; 2 months of age</li> <li>• RR <math>\geq 50</math>/min in infants 2-12 months of age</li> <li>• RR <math>\geq 40</math> in children &gt;12 months of age</li> <li>• Presence of subcostal retractions</li> </ul>	The sensitivity and specificity of tachypnea, subcostal retractions or the presence of either sign in detecting ALRI did not differ among children in different nutritional categories.
Dawson et al., 1990 <sup>36</sup>	Clinical score (mild, moderate, severe or very severe)	CXR findings (i.e., hyperinflation, atelectasis and infiltrates)	There was no correlation between CXR findings and disease severity
Mulholland et al., 1990 <sup>33</sup>	Severity at the time of admission as assessed by oximetry and arterial blood gas results  Oxygen requirements during admission	<ul style="list-style-type: none"> <li>• Demographics</li> <li>• Cyanosis</li> <li>• Crackles</li> <li>• Chest wall indrawing</li> <li>• RR &gt;50/min</li> <li>• HR &gt; 150/min</li> <li>• Liver &gt;2cm below costal margin</li> <li>• SaO<sub>2</sub> &lt;90%</li> <li>• PaO<sub>2</sub> &lt;60 mm Hg</li> <li>• PaCO<sub>2</sub> &gt;45 mm Hg</li> <li>• RSV status</li> </ul>	<p>Indicators of severity at time of admission:</p> <ul style="list-style-type: none"> <li>• young age</li> <li>• cyanosis</li> <li>• crackles</li> </ul> <p>Predictors of oxygen requirement during admission:</p> <ul style="list-style-type: none"> <li>• young age</li> <li>• cyanosis</li> <li>• crackles</li> <li>• high RR</li> <li>• chest wall indrawing</li> <li>• SaO<sub>2</sub> &lt;90%</li> <li>• PaCO<sub>2</sub> &gt;45 mm Hg</li> <li>• PaO<sub>2</sub> &lt;60 mm Hg</li> </ul>

**Table 5. Studies Measuring Predictors Of Disease Severity (continued)**

Author	Outcome predicted <sup>a</sup>	Indicators Examined <sup>b</sup>	Predictors
Shaw et al., 1991 <sup>32</sup>	"Mild disease" (defined as alert, active and able to take fluids throughout their disease, no O <sub>2</sub> therapy, etc) vs. "Severe disease" (defined as all others without mild disease)	<p>Historical information</p> <ul style="list-style-type: none"> <li>• Cyanosis or apnea</li> <li>• Gestational age &lt; 34 or 37 wks</li> <li>• Age &lt; 3 mo</li> <li>• Decreased po intake</li> <li>• Perinatal complications</li> <li>• URI symptoms &lt;3 days</li> </ul> <p>Physical examination and observations</p> <ul style="list-style-type: none"> <li>• "Ill" or "toxic" appearance</li> <li>• Yale Observation Scale <math>\geq 10</math></li> <li>• Accessory muscle use</li> <li>• Clinical Asthma Score <math>\geq 2</math></li> <li>• RR <math>\geq 60</math>/min or <math>\geq 70</math>/min</li> <li>• Rales</li> </ul> <p>Laboratory</p> <ul style="list-style-type: none"> <li>• Pulse oximetry quiet</li> <li>• Pulse oximetry while sucking</li> <li>• CXR findings of atelectasis or hyperaeration</li> <li>• Isolation of RSV</li> </ul>	<p>Six independent clinical and laboratory findings were strongly associated with more severe disease using multiple-factor analysis</p> <ul style="list-style-type: none"> <li>• "Ill" or "toxic" appearance</li> <li>• Oxygen saturation &lt; 95%</li> <li>• Gestational age &lt; 34 wks</li> <li>• RR <math>\geq 70</math>/min</li> <li>• Age &lt; 3 months</li> </ul>
Saijo et al., 1996 <sup>35</sup>	Finding of lobar pneumonia vs. bronchopneumonia vs. bronchiolitis in hospitalized infants with RSV ALRI	<ul style="list-style-type: none"> <li>• WBC &gt; 15,000/mm<sup>3</sup></li> <li>• Neutrophil count &gt; 10,000/mm<sup>3</sup></li> <li>• ESR &gt; 30 mm<sup>hr</sup></li> <li>• CRP &gt; 3.0 mg/dL</li> </ul>	The percentages of all 4 indicators were higher in patients with RSV lobar pneumonia vs. bronchiolitis or bronchopneumonia

<sup>a</sup>ALRI, acute lower respiratory infection; CXR, chest radiograph.

<sup>b</sup>RR, respiratory rate; min, minutes; HR, heart rate; WBC, white blood count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; SaO<sub>2</sub>, oxygen saturation; PaCO<sub>2</sub>, arterial carbon dioxide pressure; RSV, respiratory syncytial virus; po, oral; URI, upper respiratory infection.

**Table 6. Use of Chest X-Rays for Diagnosis of Bronchiolitis**

<b>Author</b>	<b>Purpose of Study</b>	<b>Use of Chest X-ray</b>	<b>Results</b>
Can et al., 1998 <sup>24</sup>	RCT of salbutamol vs. mist	Baseline assessment	CXR findings “consistent with bronchiolitis” were present in 88% 69% and 73% of the infants in the three study groups
Daugbjerg et al., 1993 <sup>72</sup>	RCT of nebulized terbutaline, nebulized corticosteroid and systemic corticosteroid	Baseline assessment	Infiltrates in 27% overall, no differences between 4 study groups
Dawson et al., 1990 <sup>36</sup>	Cohort design specifically to look at the utility of routine CXR's in bronchiolitis by examining the relationship between clinical assessment (i.e., mild, moderate, severe or very severe) and CXR findings (i.e., hyperinflation, atelectasis and infiltrates)	Baseline assessment	No correlation between CXR findings and disease severity
Dobson et al., 1998 <sup>37</sup>	RCT of albuterol in hospitalized infants	Baseline assessment	CXR results not reported
Friis et al., 1990 <sup>38</sup>	Prospective cohort of children < 7 years old designed to correlate CXR findings with viral and bacterial studies.	Baseline assessment	The results for children with bronchiolitis not reported separately, so no conclusions can be drawn
Luchetti et al., 1998 <sup>39</sup>	RCT of porcine-derived surfactant in ventilated infants	Baseline assessment and to document clinical improvement	CXR results not reported
Nasr et al., 2001 <sup>40</sup>	RCT of rhDNase in hospitalized infants	Baseline assessment and at study end or time of hospital discharge	CXR improvement was a trial outcome (CXR scores improved in the treatment group but not in the control group) CXR findings were not used to assess disease severity or determine management

**Table 6. Use of Chest Radiographs for Diagnosis of Bronchiolitis(continued)**

<b>Author</b>	<b>Purpose of Study</b>	<b>Use of Chest x-ray</b>	<b>Results</b>
Rodriguez et al., 1997 <sup>25</sup>	RCT of RSVIG treatment of hospitalized young children at high risk for severe disease	Baseline assessment Repeated at time of hospital discharge	CXR results not reported
Rodriguez et al., 1997 <sup>41</sup>	RCT of RSVIG treatment of previously healthy hospitalized children	Baseline assessment Repeated at time of hospital discharge	CXR results not reported
Rodriguez et al., 1987 <sup>42</sup>	RCT of ribavirin in infants with RSV disease (included patients with bronchiolitis, pneumonia, and croup)	Baseline assessment	CXR results for infants with bronchiolitis not reported separately
Roosevelt et al., 1996 <sup>43</sup>	RCT of dexamethasone in acute bronchiolitis	Baseline assessment	<ul style="list-style-type: none"> <li>• No data presented correlating CXR findings to disease severity</li> <li>• Infiltrates seen in 32% of treatment group and 20% of placebo group</li> <li>• 90% of infants with visible infiltrates were treated with antibiotics vs. 44% of those without these findings</li> </ul>
Schuh et al., 1990 <sup>44</sup>	RCT of albuterol in ED	Baseline assessment	CXR results not reported

**Table 6. Use of Chest Radiographs for Diagnosis of Bronchiolitis(continued)**

<b>Author</b>	<b>Purpose of Study</b>	<b>Use of Chest x-ray</b>	<b>Results</b>
Shaw et al., 1991 <sup>32</sup>	Prospective cohort of 228 infants designed to "Mild disease" (defined as alert, active and able to take fluids throughout their disease, no O <sub>2</sub> therapy, etc.) vs. "Severe disease" (defined as all others without mild disease)	Baseline assessment	<p>Overall</p> <ul style="list-style-type: none"> <li>• 58% had hyperaeration</li> <li>• 9% had atelectasis</li> </ul> <p>Findings in patients with "Severe" vs. "Mild" disease</p> <ul style="list-style-type: none"> <li>• Atelectasis: 21% vs. 2% (RR = 2.7, CI 1.97-3.70)</li> <li>• Hyperaeration: 69% vs. 52% (RR = 1.58, CI 1.03-2.42)</li> </ul>
Taber et al., 1983 <sup>45</sup>	RCT of ribavirin in hospitalized infants	Baseline assessment	<ul style="list-style-type: none"> <li>• Hyperinflation: 24/26</li> <li>• Peribronchial thickening: 25/26</li> </ul>

CXR, chest x-ray; RCT, randomized controlled trials; RSVVIG, respiratory syncytial virus intravenous immunoglobulin, ED, emergency department; RR, relative risk; CI, confidence interval.

**Table 7. Studies Examining Complete Blood Counts Performed**

<b>Author</b>	<b>Purpose of study</b>	<b>Use of CBC in study</b>	<b>Results</b>
Barry et al., 1986 <sup>46</sup>	RCT of ribavirin in acute bronchiolitis	Baseline assessment Completion of study	CBC results not reported
Can et al., 1998 <sup>24</sup>	RCT of salbutamol vs. mist	Baseline assessment	Mean WBC, neutrophils, eosinophils, Hgb and HCT similar in three study groups
Chippis et al., 1993 <sup>47</sup>	RCT of alpha-2A-interferon in hospitalized infants	Baseline assessment Day 5 of study	CBC results not reported
De Boeck et al., 1997 <sup>48</sup>	RCT of dexamethasone hospitalized infants	Baseline assessment	No difference in leukocyte count and eosinophilia between treatment groups
Friis et al., 1984 <sup>49</sup>	RCT of antibiotics in treatment of pneumonia and bronchiolitis	Baseline assessment	CBC results for bronchiolitis vs. pneumonia not compared
Kjølhed et al., 1995 <sup>50</sup>	RCT of vitamin A in ALRI	Baseline assessment	CBC results not reported
Kong et al., 1993 <sup>51</sup>	RCT of Chinese herbs in hospitalized infants	Baseline assessment	CBC results not reported
Rodriguez et al., 1987 <sup>42</sup>	RCT of ribavirin in infants with RSV disease (included patients with bronchiolitis, pneumonia, and croup)	Baseline assessment	No differences between treatment groups
Saijo et al., 1996 <sup>35</sup>	Finding of lobar pneumonia vs. bronchopneumonia vs. bronchiolitis in hospitalized infants with RSV ALRI	<ul style="list-style-type: none"> <li>• WBC &gt; 15,000/mm<sup>3</sup></li> <li>• Neutrophil count &gt; 10,000/mm<sup>3</sup></li> <li>• ESR &gt; 30 mm/hr</li> <li>• CRP &gt; 3.0 mg/dL</li> </ul>	The percentages of all 4 indicators was higher in patients with RSV lobar pneumonia vs. bronchiolitis or bronchopneumonia
Taber et al., 1983 <sup>45</sup>	RCT of ribavirin in hospitalized infants	Baseline assessment Time of discharge Followup	No differences between treatment groups No differences from admission to discharge to followup

CBC, complete blood count; RCT, randomized controlled trial; WBC, whole blood count; Hgb, hemoglobin; HCT, hematocrit; RSV, respiratory syncytial virus; ALRI, acute lower respiratory infection; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

**Table 8. Results of Impact RSV Trial<sup>a</sup>**

	Treatment Arm			Control Arm			Relative Rate <sup>b</sup>	P-value
<b>Hospitalization Rates</b>	#	Per	average	#	per	average		
Overall	48	1002	4.8%	53	500	10.6%	<b>0.45</b>	<.001
CLD	39	496	7.9%	34	266	12.8%	<b>0.615</b>	0.038
No CLD	9	506	1.8%	19	234	8.1%	<b>0.22</b>	<.001
> 5 kg							<b>0.49</b>	0.014
= 5 kg							<b>0.43</b>	0.001
<32 weeks gestation	43	739	5.8%	41	372	11.0%	<b>0.53</b>	0.003
32 thru 35 weeks gestation	5	263	1.9%	12	128	9.4%	<b>0.20</b>	0.002
<b>Days of Hospitalization</b>	#	Per	average	#	per	average		
	36.4	100	0.3640	62.6	100	0.6260	<b>0.58</b>	0.001
<b>Days with Oxygen</b>	#	Per	average	#	per	average		
	30.3	100	0.3030	50.6	100	0.5060	<b>0.60</b>	0.001
<b>Days with LRI score = 3</b>	#	Per	average	#	per	average		
	29.6	100	0.2960	47.4	100	0.4740	<b>0.62</b>	0.001
<b>ICU</b>								
Days			12.7000			13.3000	<b>0.95</b>	0.023
rate of admission			0.0130			0.0300	<b>0.43</b>	0.026
<b>Mechanical Ventilation</b>								
Days			8.4000			1.7000	<b>4.94</b>	0.21
rate of admission			0.0070			0.0020	<b>3.50</b>	0.28

Source: Impact RSV Study Group, 1998,<sup>91</sup> and Lofland et al., 2000.<sup>14</sup>

<sup>a</sup> BPD, bronchopulmonary dysplasia; LRI, lower respiratory infection; ICU, intensive care unit.

<sup>b</sup> Relative Rate = Treatment prevalence/Control prevalence.

**Table 9. RSV Hospitalization Rates**

Source	Entry Criteria	Year	Baseline Hospitalization		Palivizumab Hospitalization	
Very Premature						
Sorrentino and Powers 2000 <sup>101</sup>	<28 EGA	1998-99			15/445	3.4%
Cunningham et al., 1991 <sup>102</sup>	=32 EGA	1985-86	19/130	14.6%		
Impact RSV 1998 <sup>91</sup>	=32 EGA	1996-97	41/372	11.0%	43/739	5.8%
Paul et al., 2002 <sup>103</sup>	=32 EGA	1999-00			0/175	0.0%
Joffe et al., 1999 <sup>13</sup>	23 to 32 EGA, >=28 O <sub>2</sub> , discharge Sept-Nov	1992-96		24.6%		
Joffe et al., 1999 <sup>13</sup>	23 to 32 EGA, >=28 O <sub>2</sub> , discharge Dec-Aug	1992-96		10.7%		
Joffe et al., 1999 <sup>13</sup>	23 to 32 EGA, <28 O <sub>2</sub> , discharge Sept-Nov	1992-96		8.0%		
Joffe et al., 1999 <sup>13</sup>	23 to 32 EGA, <28 O <sub>2</sub> , discharge Dec-Aug	1992-96		3.1%		
Sorrentino and Powers 2000 <sup>101</sup>	28 to 33 EGA	1998-99			12/611	2.0%
Average RRR	69%			11.4%		3.6%
Less Premature						
Groothuis et al., 1995 <sup>86</sup>	=35 EGA	1989-91	13/58	22.4%		
The PREVENT Group, 1997 <sup>89</sup>	=35 EGA and/or BPD	1994-95	35/260	13.5%		
Oelberg	=35 EGA	1994-96	53/378	14.0%		
Impact RSV 1998 <sup>91</sup>	=35 EGA	1996-97	53/500	10.6%	48/1002	4.8%
Farina 2002 <sup>100</sup>	=35 EGA or BPD	1998-99	10/42	23.8%		
Impact RSV 1998 <sup>91</sup>	32 to 36 EGA	1996-97	12/128	9.4%	5/263	1.9%
Sorrentino and Powers 2000 <sup>101</sup>	32 to 36 EGA	1998-99			8/548	1.5%
Joffe et al., 1999 <sup>13</sup>	33 to 36 EGA, >=28 O <sub>2</sub> , discharge Sept-Nov	1992-96		11.0%		
Joffe et al., 1999 <sup>13</sup>	33 to 36 EGA, >=28 O <sub>2</sub> , discharge Dec-Aug	1992-96		4.4%		
Joffe et al., 1999 <sup>13</sup>	33 to 36 EGA, <28 O <sub>2</sub> , discharge Sept-Nov	1992-96		3.2%		

**Table 9. RSV Hospitalization Rates (continued)**

Source	Entry Criteria	Year	Baseline Hospitalization		Palivizumab Hospitalization	
Joffe et al., 1999 <sup>13</sup>	33 to 36 EGA, <28 O <sub>2</sub> , discharge Dec-Aug	1992-96	1.2%			
Schrand et al., 2001 <sup>98</sup>	28 to 37 EGA	1994-95	10/40	25.0%	1/61	1.6%
Sorrentino and Powers 2000 <sup>101</sup>	>35 EGA	1998-99			0/26	0.0%
<b>Average RRR</b>	<b>58%</b>		<b>7.7%</b>		<b>3.3%</b>	
<b>Diagnosed with BPD</b>						
The PREVENT Study Group <sup>89</sup>	BPD	1994-95	26/149	17.4%		
Groothuis et al., 1988 <sup>99</sup>	BPD	1985-86	11/30	36.7%		
Impact RSV 1998 <sup>91</sup>	BPD	1996-97	34/266	12.8%	39/496	7.9%
Sorrentino and Powers 2000 <sup>101</sup>	BPD	1998-99			42/1839	2.3%
<b>Average RRR</b>	<b>78%</b>		<b>16.0%</b>		<b>3.5%</b>	
<b>Average RRR for All Groups</b>	<b>66%</b>		<b>10.1%</b>		<b>3.4%</b>	

RSV, respiratory syncytial virus; EGA, estimated gestational age; BPD, bronchopulmonary dysplasia; RRR, relative risk reduction.

**Table 10. Cost Estimates used in Analyses**

	Cost of Prophylaxis	Cost of Hospitalization	Value of Parents' Missed Work	
			Hospitalization	Prophylaxis
Joffe et al. 1999 <sup>13</sup>	\$3,648	\$11,336	\$466	\$57
Lofland et al., 2000 <sup>14</sup>	\$2,754 or \$4,957	\$11,551	-	-
Schrand et al., 2001 <sup>98</sup>	\$3,968	\$19,525	-	-
Marchetti et al., 1999 <sup>96</sup> (charges)	-	\$22,773	-	-
<b>Average</b>	<b>\$3,457 or \$4,191</b>	<b>\$14,019</b>	<b>\$466</b>	<b>\$57</b>

Estimates are in August 2002 dollars.

**Table 11. 2001 Cost Per Hospitalization Avoided**

CEA	32-35 Estimated Gestational Age Population		Bronchopulmonary Dysplasia Population	
Marchetti et al., 1999 <sup>96a</sup>	Savings (minimum bound)	\$33,566 (maximum bound)	Savings (minimum bound)	\$50,999 (maximum bound)
Lofland et al., 2000 <sup>14b</sup>	\$26,439 (therapy-\$2,500)	\$59,487 (therapy=\$4,500)	\$43,614 (therapy=\$2,500)	\$87,805 (therapy=\$4,500)
Schrand et al., 2001 <sup>98</sup>	Savings (internal rates <sup>a</sup> )	\$33,565 (Impact-RSV rates <sup>c</sup> )	Savings (internal rates <sup>a</sup> )	\$61,138 (Impact-RSV rates <sup>c</sup> )
Joffe et al., 1999 <sup>104d</sup>	\$117,265 (discharge Sept-Nov)	\$328,343 (discharge Dec-Aug)	\$29,707 (discharge Sept-Nov)	\$85,995 (discharge Dec-Aug)
Computed using average hospitalization costs from CEAs, average incidence rates from Table 9	\$54,500		\$19,540	

<sup>a</sup> Converted to cost per hospital avoided with IMPact-RSV hospitalization rates for each subpopulation.

<sup>b</sup> Cost per hospital avoided based on approximating similar rate reduction as seen in IMPact-RSV for each subpopulation.

<sup>c</sup> IMPact-RSV rates calculated by substituting subpopulation rates from IMPact-RSV for the overall rates used by Schrand et al.

<sup>d</sup> 32-36 weeks EGA with less than 28 days oxygen approximating 32-35 week cohort, use of oxygen for = 28 days used as approximation of CLD cohort.

**Table 12. Summary of Evidence for Treatment of Bronchiolitis**

Evidence Table: Treatment	Size of Admissible Body of Evidence			Quality of Studies	Preponderance of Evidence Favors Treatment	Adverse Events in Treatment Group
	Number of Studies	Range of Sample Size	Total Number of Patients			
1: Nebulized epinephrine vs. nebulized saline placebo	1	29	29	Fair	Yes, for oxygen saturation rates and improvement of clinical scores, evaluated one hour after treatment <sup>52</sup>	Circumoral paleness
2: Parenteral epinephrine vs. placebo	1	30	30	Good	Yes, for respiratory assessment change score <sup>110</sup>	Unreported
3: Nebulized epinephrine vs. nebulized salbutamol or albuterol	4	24-100	195	Fair: 1 Good: 3	No, except in the study by Menon et al., for oxygen saturation rates, evaluated one hour after treatment, and for hospitalization rates <sup>22</sup>	Both increased heart rate <sup>53</sup> and decreased heart rate, <sup>22</sup> higher incidence of pallor <sup>22</sup>
4: Nebulized bronchodilators (salbutamol or albuterol) vs. oral bronchodilators, nebulized ipratropim bromide, saline placebo or no treatment	11	21-169	784	Fair: 4 Good: 5 Excellent: 2	Yes, for clinical scores 30-60 minutes post-treatment <sup>21</sup> and mean change in clinical score <sup>56</sup>	Trends towards hypoxia and respiratory distress, <sup>37</sup> significantly increased heart rates <sup>59</sup>
5: Nebulized bronchodilators vs. Ipratropium bromide vs. either agent alone and/or placebo	3	62-89	220	Fair: 1 Good: 2	No	Tremulousness, <sup>111</sup> increased heart rate <sup>64</sup>
6: Oral corticosteroids vs. placebo, with or without bronchodilators	7	28-114	406	Fair: 1 Good: 4 Excellent: 2	Yes, for hospitalization, treatment failure <sup>23,72</sup> and clinical scores <sup>23,66,68</sup>	Generally unreported or unrelated to intervention
7: Parenteral dexamethasone vs. placebo	2	29-118	147	Fair: 1 Good: 1	No	Occult blood stools among dexamethasone patients <sup>43</sup>

**Table 12. Summary of Evidence for Treatment of Bronchiolitis (continued)**

Evidence Table: Treatment	Size of Admissible Body of Evidence			Quality of Studies	Preponderance of Evidence Favors Treatment	Adverse Events in Treatment Group
	Number of Studies	Range of Sample Size	Total Number of Patients			
8: Nebulized corticosteroids vs. placebo or usual care	6	40-161	492	Poor: 1 Fair: 2 Good: 3	Some evidence favoring improvement of long-term outcomes (ranging from 9 weeks to ~1 year) <sup>73-77</sup>	Oral candidiasis <sup>77</sup> , worsened symptoms in treatment group <sup>73,74</sup>
9: Ribavirin vs. placebo	7	19-41	212	Fair: 4 Good: 2 Excellent: 1	No	Transient eyelid erythema, acute respiratory distress
10: Antibiotics vs. no treatment or other antibiotics	2	61-233	294	Poor: 1 Fair: 1	No	Not reported for bronchiolitis subgroup
11: RSVIG-IV as treatment	2	98-98	196	Good: 1 Excellent: 1	No	No difference in development of adverse events including fluid overload and respiratory distress
12: Other miscellaneous treatments)	6	13-96	274	Fair: 3 Good: 3	Variable results	Variable reporting of adverse events

**Table 13. Summary of Evidence for Prophylaxis of Bronchiolitis**

<b>Evidence Table: Treatment</b>	<b>Size of Admissible Body of Evidence</b>			<b>Quality of Studies</b>	<b>Preponderance of Evidence Favors Treatment</b>	<b>Adverse Events in Treatment Group</b>
	<b>Number of Studies</b>	<b>Range of Sample Size</b>	<b>Total Number of Patients</b>			
13: RSVIG IV vs. placebo or standard care for prophylaxis	4	116-510	1,252	Good: 3 Excellent: 1	Yes, significant reduction in severity of disease <sup>86-89</sup>	All listed adverse events <sup>86-89</sup>
14: Monoclonal antibody for prophylaxis	2	42-1486	1,528	Good: 1 Excellent: 1	Yes, significant reduction in severity of disease <sup>91</sup>	Several listed, but not significantly greater in treatment group <sup>91</sup>
15: Vaccines (Purified Fusion Protein)	3	21-34	84	Fair: 1 Good: 2	Limited reduction in severity of disease <sup>93-95</sup>	Tenderness at the vaccine site